

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/020516

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C12P19/34 C07H21/02 C07H21/04 A01N43/04  
A61K31/713

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95/09236 A (GEN HOSPITAL CORP ; HYBRIDON INC (US)) 6 April 1995 (1995-04-06) page 6, lines 11-14 claim 7; example 8	1-32, 34
Y	WO 95/32986 A (HYBRIDON INC ; AGRAWAL SUDHIR (US); MESCHWITZ SUSAN (US)) 7 December 1995 (1995-12-07) page 9, line 11 ----- -/--	1-32, 34

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

1 February 2005

Date of mailing of the international search report

10. 06. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Barnas, C

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/020516

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>ELBASHIR S M ET AL: "Functional anatomy of siRNAs for mediating efficient RNAi in <i>Drosophila melanogaster</i> embryo lysate" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 20, no. 23, 3 December 2001 (2001-12-03), pages 6877-6888, XP002225998 ISSN: 0261-4189 cited in the application page 6881, right-hand column, paragraph 2 - page 6882, left-hand column, paragraph 1 page 6884, left-hand column, paragraphs 3,4 page 6885, left-hand column, paragraph 4 - right-hand column, paragraph 1</p>	1-32,34
Y	<p>PARRISH S ET AL: "Functional anatomy of a dsRNA trigger: Differential requirement for the two trigger strands in RNA interference" MOLECULAR CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 6, no. 5, November 2000 (2000-11), pages 1077-1087, XP002226298 ISSN: 1097-2765 cited in the application figures 5,6</p>	1-32,34
Y	<p>WO 00/44895 A (KREUTZER ROLAND ; LIMMER STEPHAN (DE)) 3 August 2000 (2000-08-03) cited in the application page 6, line 30 - page 7, line 7 page 18, lines 13-29 claims 27,28,64,65,100,101</p>	1-32,34
P,X	<p>NOVIELLO C ET AL: "Autosomal recessive hypercholesterolemia protein interacts with and regulates the cell surface level of Alzheimer's amyloid Beta precursor protein" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 278, no. 34, 22 August 2003 (2003-08-22), pages 31843-34847, XP002972646 ISSN: 0021-9258 page 31844, right-hand column, paragraph 2 page 31846, left-hand column, paragraph 2; figure 5</p>	1-32,34

-/--

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>MILLER VICTOR M ET AL: "Targeting Alzheimer's disease genes with RNA interference: An efficient strategy for silencing mutant alleles." NUCLEIC ACIDS RESEARCH, vol. 32, no. 2, 2004, pages 661-668, XP002315762 ISSN: 0305-1048 abstract table 1 page 664, right-hand column, paragraph 5 - page 665, left-hand column, paragraph 2 -----</p>	1-32,34

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/020516

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1- 32, 34

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-32, 34

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1.

---

2. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 1-33, 200-232.

---

3. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 34-66, 233-265.

---

4. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 67-99, 266-298.

---

5. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 100-132, 299-331.

---

6. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 133-165, 332-364.

---

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 166-199, 365-398.

---

8. claims: 33, 35 (part)

A double stranded short interfering nucleic acid (siNA) molecule that directs cleavage of an amyloid precursor protein (APP) RNA via RNA interference (RNAi) as described in claim 1 wherein said siNA comprises any of SEQ ID NOs: 1463-1470, 1495-1590.

---

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC JS2004/020516

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9509236	A	06-04-1995	AU 7845194 A	18-04-1995
			CA 2171553 A1	06-04-1995
			CN 1136327 A	20-11-1996
			EP 0721503 A1	17-07-1996
			JP 9505465 T	03-06-1997
			NO 961262 A	28-03-1996
			WO 9509236 A1	06-04-1995
			US 5670634 A	23-09-1997
-----				
WO 9532986	A	07-12-1995	AT 188479 T	15-01-2000
			AU 2604995 A	21-12-1995
			CA 2190998 A1	07-12-1995
			DE 69514351 D1	10-02-2000
			DE 69514351 T2	10-08-2000
			EP 0763050 A1	19-03-1997
			JP 10504184 T	28-04-1998
			WO 9532986 A1	07-12-1995
			US 6489464 B1	03-12-2002
-----				
WO 0044895	A	03-08-2000	DE 19956568 A1	17-08-2000
			AT 222953 T	15-09-2002
			AU 778474 B2	09-12-2004
			AU 3271300 A	18-08-2000
			AU 2005201044 A1	07-04-2005
			CA 2359180 A1	03-08-2000
			WO 0044895 A1	03-08-2000
			DE 10080167 D2	28-02-2002
			DE 20023125 U1	15-05-2003
			DE 50000414 D1	02-10-2002
			EP 1144623 A1	17-10-2001
			EP 1214945 A2	19-06-2002
			ES 2182791 T3	16-03-2003
			JP 2003502012 T	21-01-2003
			US 2004072779 A1	15-04-2004
			US 2004053875 A1	18-03-2004
			US 2004102408 A1	27-05-2004
			US 2005100907 A1	12-05-2005
			ZA 200105909 A	24-07-2002
-----				